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FISH & RICHARDSON P.C.
225 FRANKLIN ST
BOSTON, MA 02110-2804

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,613	BELTZER ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *4, 6-11,14,16,20,33-66 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,12,13,15,17-19,21-32,67-69 and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-71* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The responses filed April 22, 2004 and May 8, 2003 have been entered into the record.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate written description support under 35 U.S.C. 112 for claims 1-71 and the specifically the elected species of invention SEQ ID NO:457, that falls with in the elected invention of Group XV directed to SEQ ID NO:448.

Specification

The disclosure is objected to because of the following informalities:

Tables 7 and 8 of the specification contain sequences with "?". The "?" is not an appropriate sequence identifier, consistent with the sequence rules. Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademarks has been noted in this application, at least pages 117, 123 and 124. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicants should check the specification for specific trademarks and amend the specification accordingly. Further, it is noted that the term "BLyS" is a trademark of

Human Genome Sciences. As such, this term must also comply with the use of trademarks in the application and in the claims. Correction is required.

Information Disclosure Statement

The information disclosure statement filed 9/3/02 has been considered to the extent of the US Patent Listed therein. A initialed copy is enclosed.

The references that are non-initialed were previously provided but apparently became detached from the back-scanned paper file and thus are not present and have not been scanned into the electronic file wrapper. The examiner requests a second copy of the missing references for consideration and scanning into the electronic file wrapper for proper consideration and completion of the legal electronic record. No fee is required with the submission of the lost references.

Election/Restrictions

Applicant's election with traverse of Group XV, Lupus, SEQ ID NO:457 and increasing BlyS-mediated lifespan of B cells in the responses filed April 22, 2004 and May 8, 2003 is acknowledged. The traversal is on the ground(s) that the restriction is improper because the search is not mutually exclusive and the peptides share the structure of SEQ ID NO:446. This is not persuasive, the alternatively recited peptides are not required to have SEQ ID NO:446 and this structure is not related by the identical mechanisms because the claims recite the alternative of inhibition/reduction or increasing/activating and as such the structure of SEQ ID NO:446 is not specifically linked to any particular mechanism, mere binding to BLyS^{TM} is not that which is required by the instant therapeutic claims 1-71. Specific activities, that are MUTUALLY exclusive are required by these claimed peptides. Each peptide is chemically distinct from the other because it defines a certain sequence of amino acids, these amino acids as currently claimed do not form a core sequence which would necessarily reveal art on the other

peptides of the restricted groups of invention. For example, SEQ ID NO:1 does not even contain the residue "Asp" as such the search of SEQ ID NO:446 is MUTUALLY EXCLUSIVE of SEQ ID NO:1. Applicants argue that the peptides share common biochemical features. This is not persuasive, the claims require activation or inhibition, these biochemical and biological functions are completely opposite and therefore similar structure does not predict similar function. The search and examination of one does not encompass the other. Applicants argue that the claimed peptides share common structural features set forth in the specification. This is not persuasive, the teachings of the specification are not read into the claims. The examination of mutually exclusive properties is not an indicia of interrelatedness and places an undue examination burden on the examiner. Applicants argue that the peptides are not mutually exclusive. This is not persuasive, the individual peptides are distinct chemical entities and are therefore patentably distinct as explained in the restriction requirement. The families of peptides are not related by structure and function in the claims How can the same peptide provide for activation and inhibition of immunoglobulin production ? As such, the families of peptides as claimed, do not share a structure in common that defines a common claimed biological property and in fact provide for peptides with the apparent opposite claimed function. The species election therefore stands. The species are not related by structure and claimed activity, the claimed activities are opposite. The opposite activities are not interrelated but mutually exclusive for examination. The requirement is still deemed proper and is therefore made FINAL.

Claims 4, 6-11, 14, 16, 20, 33-66, and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed May 8, 2003.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. § 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67, 68, 69 and 71 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a either a *specific and substantial* asserted utility or a well established utility.

The claims are drawn to (1) methods of treating preventing or ameliorating a disease or disorder associated with aberrant B Lymphocyte Stimulator (BLyS™) by administering to an animal a BLyS™ binding polypeptide; (2) a method of treating, preventing or amelioration and immune system disease or disorder comprising administering to an animal a BLyS™ binding polypeptide; (3) a method of treating, prevention or ameliorating a disease or disorder of cells of hemopoietic origin comprising administering to an animal a BLyS™ binding polypeptide; (4) a method of inhibiting or reducing immunoglobulin production comprising contacting or administering to an animal a BLyS™ binding polypeptide; (5) a method of inhibiting or reducing B cell proliferation comprising contacting or administering to an animal a BLyS™ binding polypeptide; (6) a method of inhibiting or reducing activation of B cells comprising contacting or administering to an animal a BLyS™ binding polypeptide and (7) A method of increasing lifespan of B cells comprising contacting or administering to an animal a BLyS™ binding polypeptide, wherein the disease or disorder is lupus and the binding polypeptide is SEQ ID NO:457.

The teachings of the specification are limited to families of BLyS™ binding polypeptide peptides of less than 18 amino acids that bind BLyS™ . The specification contemplates that that mere binding of BlyS ™ provides for treatment of a variety of diseases or disorders, *in vitro* or *in vivo* as recited above. The specification alleges that binding can provide for a response that is inhibited or activated. The specification discloses a host of diseases or disorders and with the exception of Lupus, which was demonstrated in the art to have increased circulating BLyS™ levels, not one of the diseases or disorders contemplated in the specification has been art associated or is

specifically described in this specification as having aberrant BlyS ™, BLyS™ receptor expression or activity. The relationship between BLyS™, its receptors or activity thereof and the plethora of diseases and disorders listed is hypothetical and lacks evidentiary support either in the art or in this specification at the time of filing and as such lacks specific utility. The specification fails to teach that any of the binding polypeptides described in the specification have the ability to modulate any biological function of BLyS™, BLyS™ receptor or activity thereof either *in vitro* or *in vivo*. The specification fails to teach, and the art is devoid of any teaching that the binding of any of the claimed polypeptides to BlyS ™ provides for any of the claimed biologically measurable activities either *in vitro* or *in vivo*. The claimed use of the BLyS™-binding polypeptides does not constitute a substantial utility because one skilled in the art would have to discover the actual biological activity of the binding polypeptide (i.e. inhibiting or activating) prior to contacting or administering to be able to distinguish modulators of activity (i.e. increasing, decreasing, activating) from null binding events. Identifying and studying the properties of the BLyS™ binding polypeptides itself for identification of the potential activity thereof *in vitro* or *in vivo* does not define a "real world" context or use. The binding of any of the short peptides disclosed herein has not been correlated with any *in vitro* assay that is predictive of *in vivo* activity. This specification is devoid of any teaching that indicates that any of the claimed BLyS™ binding polypeptides have any effect at all *in vitro or in vivo*. Binding of BLyS™ in this specification has not been correlated with modulation of any biological activity of BLyS™ or its cognate receptors. Not even the most basic of tests indicating that the Bind[ing]-binding polypeptides were able to block binding of BLyS™ to its cognate receptors has been performed. There is no data indicating that the small peptides disclosed in this specification as BLyS™-binding polypeptides have any activity at all. Binding of the peptide can have three distinct biological functional outcomes: (1) inhibition, (2) activation or (3) null (no effect at all). The specification does not teach which of these biological functional outcomes are provided by any of the claimed peptides.

As such, utility for treatment of Lupus, inhibiting/reduction of immunoglobulin production, inhibiting or reducing B cell proliferation, inhibiting or reducing activation of B cells and increasing the lifespan of B cells is not found to be a substantial utility. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, since one skilled in the art would have to determine if any of the BLyS™ binding polypeptides blocked binding to the cognate receptors in vitro and then determine if the peptides were similarly effective *in vivo*, this specification does not provide a "real world" utility. Given the lack of teachings in the specification in regard to the ability of any of the disclosed binding peptides to block any activity of BLyS™ *in vitro*, the relationship of BLyS™ or its receptor to the plethora of unrelated diseases including the elected Lupus, there is an insufficient nexus that would lead one of skill in the art to predict mere binding to BLyS™ with effective treatment or modulating BLyS™ activities or receptor activities. The specification at the time of filing does not teach a nexus between mere binding for any described peptide, and certainly not for SEQ ID NOs:448 and 457, and ANY *in vitro* effect or *in vivo* effect. One skilled in the art would have to ascertain if their was a nexus between binding of the peptides and any BLyS™ activity or BLyS™ receptor activity and then investigate if the binding polypeptides could be of use in therapy or as a means to modulate the claimed B cell activities. The listing of potential assays in the Examples to use to identify polypeptides useful for such activities does not establish that the specification defined a specific and substantial utility for the claimed Bind[ing]-binding polypeptides at the time of filing. The need for such research to delineate any actual activity for the BLyS™-binding polypeptides, before the polypeptides can be contemplated for use therapeutically as claimed, clearly indicates that the methods of using the BLyS™ binding polypeptides are not disclosed as to a currently available form or possess substantial utility. The courts have held that the disclosure is insufficient when testing is necessary to determine the actual use or possible lack of use *(In re Kirk and Petrow*

(CCPA) 153 USPQ 48). The court has held that "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exist in currently available form-there is insufficient justification for permitting an application to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion." Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1996).

Note, because the methods of use of the BLyS™ binding polypeptides of claimed invention are not supported by a specific and substantial asserted utility or well established utility for the reasons set forth above, credibility has not been assessed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67, 68, 69 and 71 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to the use of a BLyS™ binding polypeptides that bind BLyS™. The specification defines a BLyS™ binding polypeptide as a molecule that can bind a BLyS™ target protein. The term BLyS™ target or BLyS™ target protein is defined to encompass BLyS™ and BLyS™-like polypeptides (specification page 20). BLyS™-like polypeptides are defined by the specification to encompass natural BLyS™ or full-length recombinant BLyS™ as well as fragments and variants such as modified or truncated forms and retain a functional activity of BLyS™ (specification paragraph bridging pages 19-20). The teachings of the specification are limited to polypeptides that bind an undefined recombinant BLyS™ that was obtained from Human Genome Sciences (see Example 1 of the specification). There is no indication that these peptides broadly bind all

natural BlyS proteins. Further, while the art and the specification teaches natural mammalian BlyS proteins, the specification does not teach any variants and a representative number of fragments of such natural proteins that retain any activity of BLyS™ as defined in the specification. The variants encompass polypeptides that have no structure in common with the natural BLyS™ polypeptides described herein. As such, the specification fails to adequately describe the use of the claimed genus of BLyS™ binding polypeptides that bind these BLyS™-like variants because none are described in this specification. The specification does not place any structure, chemical or functional limitations on the variants of BLyS™-like polypeptides. The recitation of "BLyS™-like" does not convey a common structure or function. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification teaches that variants can be readily screened, the specification and the claim do not provide any guidance on the structure of the polypeptide and what changes can or can not be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus of peptides. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure fails to describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function an activity in common" alone is insufficient to describe the genus of BLyS™-like polypeptides of that function equivalently. Consequently, the specification can not and does not provide adequate written description for the binding polypeptides that bind of BLyS™-like polypeptides or natural BLyS™ polypeptides that were not the same structure as that provided by Human Genome Sciences in Example 1 of the specification). Applicants were not in possession of the claimed genus of polypeptides that bind BLyS™ because the specification does not

describe variants of natural BlyS, BLyS™-like polypeptides and specific polypeptides that bind them. Because the specification does not convey to one of skill in the art a representative number of variants in structure and function of any such polypeptide that has the claimed/structure and function. The genus of BLyS™ binding polypeptides with the claimed function is substantial and highly variant because the polypeptides do not have a common structure and function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptides (BLyS™ binding) and one skilled in the art would not recognize that applicants had possession of the genus of claimed polypeptides for use in the methods as instantly claimed.

Claims 21-24, 29, 31, 67 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of the recited claims, the claims require "contacting and effective amount of BLyS™ binding polypeptide with BLyS™. However, in order to inhibit/reduce a B cell activity or increase the life span, B cells themselves must be present. Therefore, mere contacting of BLyS™ binding polypeptide with BLyS™ does not provide for any activity but binding. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore,

the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Before setting out the art rejections. The examiner takes official notice that the art in this technology clearly indicates that the molecule described in this specification as BLyS™, is also alternatively known in the art as BAFF, TALL-1, THANK and zTNF4 as evidenced by Dorner et al (Arthritis Research, 3(4):197-199, 2001).

Claims 1, 2, 3, 12, 13, 17, 18, 19, 21, 25, 29, 30, 31, and 32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Browning et al (WO 00/43032, published July 27, 2000).

Browning et al teach methods of: (1) inhibiting B-cell growth in an animal comprising administering a therapeutically effective amount of an anti-BAFF ligand molecule or an antibody specific for BAFF ligand, (2) methods of inhibiting immunoglobulin production in an animal comprising administering a therapeutically effective amount of an anti-BAFF ligand molecule or an antibody specific for BAFF ligand, and (3) a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a composition an anti-BAFF ligand molecule or an antibody specific for BAFF ligand. (see claims 11, 12 and 17 pages 48-49). The teachings of Browning et al as they relate to an anti-BAFF ligand or antibody specific for BAFF ligand (i.e. antibodies inherently bind their targets) anticipate the instantly claimed invention.

Claims 21-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Yan et al (Nature Immunology, 1(1):37-41, July 2000).

Yan et al teach that *in vitro* soluble TACI-Fc fusion protein blocked BLyS™ induced activation in B lymphoma cells and IgM production in peripheral blood B cells. *In vivo*

treatment of immunized mice with TACI-Fc inhibited production of antigen-specific IgM and IgG1 antibodies and abolished splenic germinal center formation. As such, the teachings of Yan et al anticipate the instantly claimed invention, because the TACI-Fc fusion protein binds BLyS™ and is therefore a BLyS™ binding polypeptide. As such, the methods of using the soluble TACI (a binding protein for BLyS™) anticipate or inherently anticipated the claimed inventions.

Claims 21-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Xia et al (J.Exp.Med., 1(3):137-143, July 3, 2000).

Xia et al teach that soluble TACU extracellular domain specifically blocks TALL-1 mediated B cell proliferation in vitro (page 140, Figure 3). Xia et al teach that soluble TACI inhibits antibody production to both T cell-dependent ant T cell-independent antigens *in vivo* (see pages 140-141 and Figure 4). As such, the methods of using the soluble TACI (a binding protein for BLyS™) anticipate or inherently anticipated the claimed inventions.

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19, 29, 30, 31, and 32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gross et al (Nature, 404:995-999, April 27, 2000).

Gross et al teach that treatment of the lupus mouse with soluble TACI-IG fusion protein inhibits the development of proteinuria, prolongs the survival of the animal and reduces the number of B cells. Gross et al also teach that TAC-Ig preventing zTNF4 to human B cells and well as its stimulatory effective on murine and human B cells in vitro (see abstract). As such, the methods of using the soluble TACI (a binding protein for BLyS™) anticipate or inherently anticipate the claimed inventions.

Claims 1, 2, 3, 12, 13, 17, 18, 19, 29, 30, 31, and 32 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Shu (U.S. Patent No. 6,475,987, issued Nov 5, 2002, filed May 5, 2000 with claimed priority to US provisional applications filed on May 6, 1999 and May 1, 2000).

Shu teaches that soluble BCMA (the binding receptor for TALL-1) inhibits TALL-1 binding to Bjab cells and inhibits TALL-1 triggered B lymphocyte proliferation. (see column 46, Example 4). Shu teaches that the method of the present invention is the inhibition of B lymphocyte proliferation, activation and survival effective to inhibit B lymphocyte associated autoimmune disease. (column 6, line 54 to column 7, line 2) As such, Shu et al anticipates the instantly claimed inventions.

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19 and 21-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Theill et al (U.S, Patent Application Publication 2002/0081296, published June 27, 2002, filed May 14, 2001 with claimed priority to US provisional applications filed May 12, 2000 and June 27, 2000).

Theill et al teach compositions and methods for the treatment of immune-related and inflammatory, autoimmune and other immune-related diseases or disorders, such a rheumatoid arthritis, Chron's disease, lupus, graft versus host disease as well as treatment of lymphoproliferative diseases and other cancers (see specification at [0002]). Theill et al teach that sBCMA (i.e. a receptor that binds BlyS ^{TM}) ameliorates T cell dependent and T cell independent humoral immune responses *in vivo*. Theill et al also teach that sTACI (i.e. another receptor that binds BLyS^{TM}) also inhibits T cell dependent and T cell independent immune response *in vivo*. In addition sBCMA reduces lymphoma and colon carcinoma cell tumor growth *in vivo* and that sBCMA increases survival and reduces incidence of proteinurea and development of anti-dsDNA antibodies in an animal model of lupus. (see specification at [0012]). Theill et al teach that immunoglobulin production is inhibited (see Figure 22, Figure 25, Figure 27, Figure 28, Figure 29, Figure 32, Figure 34,

Figure 39, Figure 40, Figure 41 and [0258]-[0322]) by administration of the soluble receptor fusions.

Status of the Claims

Claims 1, 2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67, 68, 69 and 71 stand rejected. All other claims have been withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 am - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy, Ph.D.
Primary Examiner
Art Unit 1645